Where do the drugs go?

July 27 2010

Drug delivery inside the body is a complicated process. Compounds travel through a maze of aqueous solutions, lipid membranes, and barriers between the blood and tissues like the brain. Research reported in the American Institute of Physics publication the *Journal of Chemical Physics* presents a theoretical model that accurately predicts the hydration free energy (HFE) of a wide variety of organic compounds.

"HFE determines solubility and allows accurate prediction of a compound's path in a complex environment," says author Maxim Fedorov of the Max Planck Institute for Mathematics in the Sciences. "For example, in passive transport, you want to know that the compound will cross a lipid layer into the aqueous environment inside a cell rather than moving back into the surrounding aqueous environment."

Unfortunately, HFE is not measured easily or quickly, so it is available for only about a thousand of the 20 million known organic compounds. Standard prediction methods are inaccurate. The new model used a database of about 50 known HFE values to build a theoretical model using computational hydration thermodynamics and chemo-informatic techniques. "Our predictions are accurate and very cheap computationally, requiring only 10 to 20 seconds on a PC," says Fedorov.

The ultimate goal is to predict the movement of a compound in a complex environment and to screen large databases of candidate compounds for desirable characteristics. In addition to the pharmaceutical applications, Fedorov sees potential application in

modeling the environmental flow of agricultural chemicals or industrial pollutants.

More information: The article, "Accurate calculations of the Hydration Free Energies of Drug-like Molecules using the Reference Interaction Site Model" by David S. Palmer, Volodymyr P. Sergiievskyi, Frank Jensen, and Maxim V. Fedorov will be published in July in the Journal of Chemical Physics. See: jcp.aip.org/

Provided by American Institute of Physics